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2.5 HUMAN HEALTH INDICATORS

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2.5 HUMAN HEALTH INDICATORS[1]

This chapter summarizes reviewer discussions and presents consensus conclusions and recommendations for EPA's proposed human health indicators. The chapter is divided into four sections. The first three cover indicators in particular topic areas: health status, human disease and conditions, and biomeasures of exposure. The fourth discusses reviewers' responses to general questions.

The following table shows the reviewers' overall recommendations for these indicators.

Table 2.5-1. Peer Reviewer Recommendations for Human Health Indicators

Indicators	Include with Suggested Modifications	Don't Include Unless Critical Modifications Are Made	Don't Include
Health Status			
Life expectancy	✔		
Infant mortality	✔		
General mortality	✔		
Human Disease and Conditions			
Cancer incidence and mortality	✔		
Cardiovascular disease (CVD) mortality	✔		
Asthma mortality and prevalence	✔		
Chronic obstructive pulmonary disease (COPD) mortality	✔		
Infectious gastrointestinal diseases and arthropod-borne disease prevalence	✔		
Low birthweight (LBW)	✔		
Birth defect incidence and mortality	✔		
Childhood cancer incidence and mortality	✔		
Childhood asthma mortality and prevalence			✔
Preterm delivery	✔		
Biomeasures of Exposure			
Blood lead level	✔		
Blood mercury level	✔		
Blood cadmium level	✔		
Blood persistent organic pollutants (POPs) level	✔		
Urinary pesticide/herbicide level	✔		
Phthalate exposure	✔		

[1] At the time of this peer review, EPA intended to publish the ROE Technical Document in 2006. Therefore, this summary of reviewer discussions refers to the "2006 Report on the Environment" and "ROE06." These terms are synonymous with all references to the "2007 Report on the Environment" and "ROE07" elsewhere in this report.

2.5.1 HEALTH STATUS

2.5.1.1 Life Expectancy

Reviewed by the Human Health Group

Consensus Statements	
Overall recommendation	**Include with modifications.**
Critical modifications	None.
Suggested modifications	• EPA should track life expectancy from age 1 year instead of at birth. • EPA should add a data summary table, with race and ethnicity breakdown.
Other comments	None.

The peer reviewers agreed unanimously, with little discussion, that Life Expectancy is an excellent indicator of overall health and is therefore useful in answering health chapter Question 1 (What are the trends in health status in the U.S.?). As articulated by two reviewers, this is a composite indicator integrating all causes of death making it a very good proxy of health and in providing an overall picture of health. It reflects changes in the crude death rate, age-adjusted mortality, infant and childhood mortality, and in childhood and adult disease. Peer reviewers noted that the indicator is particularly useful for tracking possible sharp changes in trends.

The peer reviewers provided, however, two recommendations for improving this indicator:

- Because infant mortality is serving as a separate indicator in answering the same question, two peer reviewers recommended that EPA track life expectancy from age 1 year instead of life expectancy at birth. This disentangles the Life Expectancy indictor from the Infant Mortality indicator. Another option would be to present the data both ways.
- One peer reviewer strongly suggested that racial and ethnic trends be presented separately in tabular format, noting that large racial disparities exist. The other reviewers agreed.

2.5.1.2 Infant Mortality

Reviewed by the Human Health Group

Consensus Statements	
Overall recommendation	**Include with modifications.**
Critical modifications	None.
Suggested modifications	• EPA should display race and ethnicity data. • "What the data show" in the indicator write-up focuses on birth defects as a cause of infant mortality. The following points need to brought out: 1) disorders related to short gestation and low birth weight are the most significant cause for certain minority populations and 2) sudden infant death syndrome (SIDS) and what is known about the role of the environment.
Other comments	None.

The peer reviewers agreed unanimously that Infant Mortality is an excellent measure of overall health in a population and should be included as an indicator in answering health chapter Question 1. As noted by two reviewers, infant death rate is among the best indices of community health; it is an important indicator of progress in health care, public health, and environmental health. Two reviewers especially liked the graphic displays, but recommended that additional displays be added with race and ethnicity breakdowns. A synopsis of the brief peer reviewer discussion on Infant Mortality indicator follows.

- Peer reviewers noted that infant mortality is a valid indicator of overall health trends, but includes many variables that are not related to the environment.
- One reviewer recommended presenting race and ethnic trends separately, noting that large racial disparities exist, which are likely to have some relationship to differences in environmental condition. Others agreed.
- One reviewer commented that the indicator write-up presents malformations as the number one cause of infant death, but that disorders related to short gestation and low birth weight can be the most significant cause of infant death, particularly for certain minority populations. This point should be brought out. Others agreed.
- Two reviewers recommended that the indicator write-up discuss SIDS more clearly, including known or suspected environmental risk factors (e.g., temperature, environmental tobacco smoke, air pollution, sleeping position). Others agreed.

2.5.1.3 General Mortality

Reviewed by the Human Health Group

Consensus Statements	
Overall recommendation	**Include with modifications.**
Critical modifications	• The overall utility of this indicator is questionable. More specificity is needed. This indicator only represents a crude "count" of the number of people who died. • Leading causes of death are useful, but EPA should use years of potential life lost (YPLL) instead of a crude ranking of death. *If EPA is unwilling to use YPLL (or some other indicator that addresses this concern), then this indicator should be eliminated.*
Suggested modifications	None.
Other comments	None.

The peer reviewers questioned the overall usefulness of General Mortality as a health indicator. Generally, the reviewers indicated that the usefulness of General Mortality is limited because it is not sensitive to differences in age distribution within the population. At the onset of discussions, one peer reviewer expressed relatively strong views that General Mortality not be included as an indicator. Other reviewers expressed mixed views. After some discussion, the group agreed unanimously that this indicator be retained only if EPA uses YPLL, which they stated is better than using a crude count or ranking of death. The discussion points that led to this recommendation are highlighted below.

- Two peer reviewers emphasized that general mortality is a crude count of death and "does not really tell us anything." Another reviewer agreed that General Mortality is crude, but said it is still a powerful measure of overall health status trends.
- One peer reviewer noted that the trend is moving away from ranking leading causes of death as a measure of health status because it is biased toward reporting the causes of death occurring in older individuals. Is EPA's agenda to show trends due to the shifting age of the population? These statistics do not inform us of when people are dying of various causes, which would be more informative.

  Three reviewers commented that the reported leading causes of death are not specific to possible environmental causes, but one of these reviewers did not object to retaining this overall ranking. One reviewer specifically questioned why the overall top ten causes of death are considered rather than causes believed to be environmentally induced.
- All peer reviewers agreed that more precise measures be used. They recommended using YPLL, noting that one might be able to tease out environmentally induced diseases in some cases where YPLL increased. One reviewer suggested that EPA consider other comparable indicators, such as the disability-adjusted life year (DALY).
- Regarding the use of mortality statistics, one reviewer commented that the indicator write-up implies a greater certainty about the use of death certificate data than actually exists. In addition, there are great uncertainties in intercensal population estimates, which can impact conclusions about trends in data sets. Uncertainties also are created by incorrect coding of cause of death and underlying cause of death on death certificates, as well as by low rates of autopsies by qualified coroners. Others agreed.

[*See also peer reviewer responses to General Question 1 for additional opinion on the limitations of using mortality data.*]

2.5.2 HUMAN DISEASE AND CONDITIONS

2.5.2.1 Cancer Incidence and Mortality

Reviewed by the Human Health Group

Consensus Statements	
Overall recommendation	**Include with modifications.**
Critical modifications	• EPA should be tracking cancer incidence and not mortality. Trends in cancer mortality are largely influenced by advances in treatment, not by incidence or environmental exposures.
Suggested modifications	• EPA should track organ-specific cancers instead of overall cancer incidence, consistent with papers by Bailar (1997), Dinse et al. (1999), Schottenfeld (2005), and others who have reviewed the weight of evidence with regards to which cancers are more likely to have environmental risk factors (e.g., breast, prostate, bladder, non-Hodgkins lymphoma, brain, leukemia). Specify the primary site of origin only (e.g., leukemias), not the subtype (e.g., acute myelocytic leukemia).
Other comments	None.

After a short discussion, peer reviewers unanimously agreed that Cancer Incidence is an appropriate and useful indicator of human disease and condition and serves to answer health chapter Question 2 (What are the trends in human disease and conditions for which environmental pollutants are thought to be risk factors?). The indicator covers an area of increasing importance, and reflects the impact of cancer on the population. Further, many cancers are thought to be environmental in origin. The peer reviewers also unanimously agreed, however, that cancer mortality not be included as part of this indicator and that cancer incidence be expanded to include organ-specific cancers. A summary of peer reviewer discussions leading to these recommendations follow, including concerns voiced about regional mortality data displays.

- **Incidence over mortality**. Mortality trends often do not accurately reflect disease trends. One reviewer provided the example of increasing incidence in childhood leukemia, but decreasing mortality from this disease. This is one example of how advances in treatment and medical intervention affect mortality more than triggers of the disease, therefore in such cases making incidence a better measure of trends in the disease. All reviewers agreed. [*See also peer reviewer responses to General Question 1 for additional opinion on the limitations of using mortality data.*]
- **Including organ-specific cancers**. One reviewer strongly stated that cancer should not be classified as a single disease. General cancer incidence rates mask the variation in incidence of cancers according to organs where abnormal cellular growth begins; therefore, and the indicator should be modified to include organ-specific cancers. Others agreed. EPA should use documentation in the scientific literature to hone in on those cancer types believed to be associated with environmental pollutants. Three citations for EPA consideration were provided—Bailar (1997), Dinse et al. (1999), and Schottenfeld (2004)—but the reviewers encouraged EPA to further research the scientific literature in efforts to identify cancers that are the most likely to have environmental risk factors.

Reviewers noted that site-specific cancers are tracked in the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) database, the data source for this indicator. Reviewers discussed and agreed that EPA should include statistics for the site of origin only, not the subtypes of the cancers or secondary sites.

- **Regional trend data (Figures 076-1 and 076-2)**. The peer reviewers all voiced concern about the presentation of regional trend data for cancer mortality. The regional rates are not clearly readable (076-1) and are not especially useful. In addition, the basis for the selection and display of quartiles in the U.S. map (076-2) is not described adequately. One reviewer noted that state-by-state data would be more useful. [*See also peer reviewer responses to General Question 1 for overall comments on regional trend data compilation and presentation.*]

References

Bailar JC. 1997. Winning the war on cancer. N Engl J Med; 337:935-39.

Dinse GE, Umbach DM, Sasco AJ, Hoel DG, Davis DL. 1999. Unexplained increases in cancer incidence in the United States from 1975 to 1994: possible sentinel health indicators? Annu Rev Public Health; 20:173-209

Schottenfeld D. 2004. Principles and application of cancer prevention. In: Schottenfeld D, Fraumeni JF eds. Cancer Epidemiology and Prevention. New York: Oxford Press.

2.5.2.2 Cardiovascular Disease (CVD) Mortality

Reviewed by the Human Health Group

Consensus Statements	
Overall recommendation	**Include with modifications.**
Critical modifications	• EPA should include CVD prevalence as part of the CVD indicator. Prevalence is a better measure of the CVD than mortality. CVD prevalence data are available through the National Health Interview Survey (NHIS).
Suggested modifications	• The indicator write-up should: o Emphasize that quality and access to health care play a major role in CVD mortality. Further, the cause of death is often recorded as respiratory infection or heart attack, not the underlying disease. o Acknowledge the limitations of death certificates. o Emphasize the significance of smoking and environmental tobacco smoke (ETS) in CVD. • Figure 078-1 (CVD mortality) should be eliminated, showing just the breakdown of CVD into CHD mortality (Figures 078-2) and stroke mortality (Figure 078-3).
Other comments	None.

None of the peer reviewers questioned or objected to the inclusion of CVD as an indicator. The reviewers acknowledged that tracking CVD morbidity is important because of known and suspected environmental

links, but also agreed that tracking is "noisy" because non-environmental factors also contribute to the disease. However, the peer reviewers agreed unanimously that EPA also should include CVD *prevalence* because it is a better measure of CVD than mortality. The rationale for the peer reviewer recommendation along with other suggested revisions are summarized below.

- **Tracking CVD prevalence**. One reviewer noted that early death from CVD is a good indicator of overall health, but all agreed that many factors attribute to mortality other than environmental causes (e.g., access and quality of medical care). As one reviewer stated, death is only a crude measure of CVD. Therefore the group agreed that it is critical for EPA to consider CVD prevalence as well as mortality. One reviewer noted that the "Six Cities Study" (e.g., Dockery et al., 1993) presents mortality data, providing one argument for using mortality over prevalence data. The peer reviewers also pointed to the Health Effects Institute's reanalysis of the Six Cities Study (HEI, 2000). [*See also peer reviewer responses to General Question 1 for additional opinion on the limitations of using mortality data.*]
- **Suggested indicator write-up modifications.** The peer reviewers suggested that EPA revise the write-up to more strongly reflect the following:
  - The reasoning for including both morbidity and mortality data.
  - The limitations of mortality data (e.g., limits of using death certificate records, possible underreporting of CVD as cause of death).
  - The role of smoking and ETS in CVD.
- **Graphical displays.** The peer reviewers questioned why EPA displayed aggregate CVD mortality data (Figure 078-1) and disaggregated data (Figures 078-2 and 078-3). While some did not object one way or the other, one reviewer did not believe that there was any value in lumping together the data for different types of CVD. Further, prevalence data are not available as a composite, which makes the presentation of types of CVD preferable (e.g., coronary heart disease, stroke). [*See also peer reviewer responses to General Question 1 for broader comments on regional trend data compilation and presentation.*]

References

Dockery DW, Pope CA 3rd, Xu X, Spengler JD, Ware JH, Fay ME, Ferris BG Jr, Speizer FE. 1993. An association between air pollution and mortality in six U.S. cities. N Engl J Med. 329(24):1753-9.

[HEI] Health Effects Institute. 2000. Reanalysis of the Harvard Six Cities Study and the American Cancer Society Study of Particulate Air Pollution and Mortality. A Special Report of the Institute's Particle Epidemiology Reanalysis Project. Final version, July 2000.

2.5.2.3 Asthma Mortality and Prevalence

Reviewed by the Human Health Group

Consensus Statements	
Overall recommendation	**Include with modifications.**
Critical modifications	• EPA should combine adult and childhood asthma into a single indicator. The disease is a continuum over a lifetime. Most adult asthma can be traced to early life exposures, with the exception of occupational triggers.
Suggested modifications	• EPA should be tracking asthma prevalence and not mortality. Trends in asthma mortality are influenced largely by advances in treatment, not by prevalence or environmental exposures. Although environmental conditions exacerbate asthma, most asthma-related deaths are completely preventable with appropriate medical treatment. Asthma prevalence and attack are more related to the environment (both ambient and indoor). • EPA should display demographic breakdown, including race and ethnicity data. • EPA should present the childhood asthma prevalence in smaller age categories (now 0-17 years), because the prevalence is higher in younger children and because rates in younger children (0-4 years) may be a more sensitive indicator of environmental change. • Because the asthma case fatality rate is low, trend data for asthma mortality are not robust, especially when broken down into 10 EPA regions. This underscores the reviewers' recommendation not to track mortality.
Other comments	None.

Peer reviewers unanimously agreed that Asthma Prevalence is an appropriate and important indicator of human disease and condition and serves to answer the question it is intended to answer. Asthma attacks can be triggered by environmental insult, and gene-environment interaction may account for a notable portion of the risk for developing asthma initially and the severity of attacks that may occur. However, the peer reviewers unanimously agreed that EPA should not track Asthma Mortality, nor should they track adult asthma separately from childhood asthma. Peer reviewers also recommended some modifications to how EPA presents trend data. Highlights of peer reviewer discussions and the rationale for their recommendations are presented below.

- **Combining adult and childhood asthma**. One reviewer pointed out that asthma is a disease viewed as a continuum over a lifetime. Most asthma can be traced to early life exposures, with the exception of occupational triggers. Based on this statement, the reviewers agreed that EPA should present asthma as a single indicator.
- **Tracking asthma prevalence, not mortality**. With little discussion, peer reviewers agreed that asthma mortality is not a useful or meaningful indicator. Asthma mortality is a rare outcome, and is driven entirely by treatment, not environmental factors. The group therefore agreed that EPA should use prevalence data only for this indicator. [*See also peer reviewer responses to General Question 1 regarding general limitations associated with the use of mortality data.*]

- **Age, gender, race/ethnicity breakdowns.** The peer reviewers encouraged EPA to provide further demographic breakdowns for this indicator. Specifically, one reviewer recommended breaking out age groups, gender, and race/ethnicity similar to Table 098_105Lead. Though the reviewers recommended combining adult and childhood prevalence data, age groups should be clearly separated out. Further, one reviewer suggested and others agreed that childhood asthma prevalence be reported separately for younger children (0-4 years) because this age group may be a more sensitive indicator of environmental change.
- **Temporal trends.** The reviewers stated that the displays showing temporal trends for Asthma Prevalence are useful and should be retained. However, one reviewer commented that the smoothed curves in Figures 082-1 and 082-2 mislead: only the points given in the graph exist, not the curvature between the points. It is important to distinguish between period and point prevalence.
- **Regional trends**. The peer reviewers stated unequivocally that the presentation and the logic behind the regional displays were poor. For example, what does it really mean if one region has an age-adjusted asthma mortality rate of 1.2 versus 1.8 per 100,000? Little useful information is gained, especially with mortality rates being so low for asthma. [*See also peer reviewer responses to General Question 1 for broader comments on regional trend data compilation and presentation.*]

2.5.2.4 Chronic Obstructive Pulmonary Disease (COPD) Mortality

Reviewed by the Human Health Group

Consensus Statements	
Overall recommendation	**Include with modifications.**
Critical modifications	• EPA should include COPD prevalence as part of the COPD indicator. Prevalence is a better measure of COPD than mortality. COPD prevalence data are available through NHIS—chronic bronchitis (Code 601) and emphysema (Code 609) can be combined.
Suggested modifications	• The indicator write-up should: o Emphasize that access to and quality of care play a major role in COPD mortality. Further, cause of death is often recorded as respiratory infection or heart attack, not the underlying disease. o Acknowledge the limitations of death certificates. o Emphasize the significance of smoking and ETS in COPD. • For clarity, EPA should consider labeling the indicator as "Chronic Obstructive Lung Disease" instead of COPD.
Other comments	None.

Peer reviewers all agreed that COPD is an important and appropriate indicator because of the known and suspected association between environmental exposures and this group of diseases (e.g., particulates, sulfur dioxide, and cadmium). However, the reviewers expressed a strong opinion that prevalence is a better measure of COPD than mortality and should be included as part of the COPD indicator.

- **Tracking COPD prevalence**. Peer reviewers agreed that prevalence provides more information about COPD than does mortality. People can survive a long time with COPD. One reviewer

emphasized the large role that cigarette smoking plays in COPD, particularly in industrialized countries; Barnes (2000) offers perspective on the issue and acknowledges that precise numbers on prevalence are surprisingly scant. The reviewers recommended that EPA seek prevalence data through NHIS, specifically recommending that chronic bronchitis (Code 601) and emphysema (Code 609) be used.

- **Suggested indicator write-up modifications.** As with the CVD indicator, the peer reviewers suggested that EPA revise the write-up to more strongly reflect the following:
  - The reasoning for including both morbidity and mortality data.
  - The limitations of mortality data (e.g., limits of using death certificate records, possible underreporting of COPD as cause of death).
  - The role of smoking and ETS in COPD.
- **Changing the indicator label.** One peer reviewer suggested and others agreed that the indicator label "Chronic Obstructive Pulmonary Disease" would be more user-friendly if it were "Chronic Obstructive Lung Disease."

References

Barnes PJ. 2000. Chronic obstructive pulmonary disease. N Engl J Med. 343(4):269-80.

2.5.2.5 Infectious Gastrointestinal Diseases and Arthropod-Borne Disease Prevalence

Reviewed by the Human Health Group

Consensus Statements	
Overall recommendation	**Include with modifications.**
Critical modifications	• EPA should split the indicator into two indicators: infectious gastrointestinal diseases and arthropod-borne diseases. • EPA should not refer to available measures of disease as prevalence. Refer to the "number of reported new cases," *not* prevalence.
Suggested modifications	• Though stated in the indicator write-up, EPA should emphasize more strongly the likely underreporting or possible misreporting of gastrointestinal diseases. EPA should also emphasize that reported cases are not measures of disease burden. In other words, it should be made clear that these indicators are useful for tracking trends but are not absolute numbers. • EPA should display reports of the individual diseases on separate graphs or in tabular format because rates vary. Log scale is not appropriate for this presentation; it distorts the data. • EPA should give thorough consideration to including the following reportable infectious diseases: o Gastrointestinal diseases: Giardia and cyclosporidia, both of waterborne origin and associated with exposure through contaminated irrigation water. o Arthropod-borne diseases: Malaria, dengue, and viral encephalopathies other than West Nile Virus. Competent vectors are abundant in the U.S. (CDC, 2005). o Legionellosis: Legionella are found in indoor air and should be tracked in a separate category. o Zoonotic (animal-borne) diseases: Hantavirus, plague, and rabies. EPA should assess major zoonotic diseases over time. If they are becoming more widespread, EPA should consider adding them as indicators.
Other comments	None.

At the start of discussions, one peer reviewer recommended not including reportable infectious diseases as an ROE06 health indicator, though after a relatively lengthy discussion the peer reviewers unanimously agreed that this indicator should be retained. Reviewers agreed that gastrointestinal disease prevalence is an overall indicator of environmental condition (e.g., water quality) and changes in arthropod-disease provide some indication of changes in local weather conditions. Further, one reviewer emphasized the observed resurgence of arthropod-borne disease. However, the group strongly recommended a number of modifications to improve the presentation and utility of this indicator set, including a breakout of the classes of reportable disease and adding more diseases. Specific topics discussed by the peer reviewers and the rationale for their final conclusions and recommendations are highlighted below.

- **Remove reference to disease "prevalence."** Peer reviewers agreed that EPA should refer to "reported new cases," not prevalence. Available data report incidence, not disease rates.

- **Most relevant reportable diseases.** One reviewer opened discussions by breaking infectious diseases out as follows, suggesting that the group consider the most appropriate diseases for indicator inclusion: (1) gastroenteritis (foodborne, waterborne), (2) vector-borne (mosquitoes, tick-borne), (3) legionellosis (indoor air), and (4) zoonotic (rodents, dogs, cats).

  At a minimum, the group agreed that the indicator should be divided into two pieces: gastrointestinal and arthropod-borne (vector-borne diseases). The group generally agreed that inclusion of these disease categories was appropriate. They noted that EPA included the most relevant diseases in these categories, but questioned some and recommended adding others.

  - Gastrointestinal: One reviewer questioned the value of monitoring cholera based on the very small number of cases reported each year. Such small numbers cannot indicate a trend.No recommendation to remove it was made, however. One reviewer suggested and others agreed that EPA consider including giardia and cyclosporidia—both of water-borne origin.
  - Arthropod-borne: Three of the four peer reviewers initially agreed that EPA should track arthropod-borne disease as a measure of environmental condition such as climate change. One reviewer noted that such tracking might identify environmental disturbance. One reviewer argued, however, that arthropod-borne disease prevalence is not a strong indicator and likely to be indicative of local weather conditions only. After agreement by all that EPA should be tracking trends with a particular eye toward the future, the peer reviewers suggested that EPA consider adding malaria, dengue, and the mosquito-borne viral encephalopathies other than West Nile virus. One reviewer commented that competent dengue vectors, for example, are abundant in the United States.

  The peer reviewers also discussed whether EPA should consider including legionellosis and zoonotic diseases. The group agreed without discussion that legionellosis should be added because of its presence in indoor air. Initially, the group expressed disparate views on zoonotic diseases, some noting that animal-borne diseases were not an indicator of environmental trends while others noted that said diseases could be indicative of ecological shifts. The entire group agreed that EPA should not add zoonotic diseases as indicators in ROE06, but should monitor trends in diseases, such as hantavirus, plague, and rabies; if trend analysis suggests that one or more of these diseases are becoming more endemic due perhaps to climate change, EPA might want to consider adding this disease group as a future indicator.

  Regardless of what indicators EPA includes, the group agreed, the indicator write-up and/or supporting text needs to be more transparent on how EPA selected the individual diseases included as part of this indicator set.

- **Stronger acknowledgement of data limitations.** One reviewer expressed concern overall that the small number of reported cases of many of these diseases limits the overall utility of the indicator set. Further, the prevalence of these diseases is likely to be of interest in limited geographic locations and for limited times rather than on a national basis.

  Another reviewer emphasized and others echoed the importance of clearly articulating the fact that the number of reported infectious disease cases is likely very much under-reported. One reviewer clarified that these infections often go undiagnosed or misdiagnosed. Such diseases, if diagnosed properly, are likely to be reported; but if someone has a “stomach flu” that really was giardiasis, no one will ever know. The indicator write-up could be stronger in explaining this fact. Further, EPA should strongly state that the indicators are useful for tracking trends, but do not represent absolute disease burden. This is especially noteworthy when “trends” may represent trends in reporting criteria rather than trends in actual cases. This is similar, in a sense, to reporting asthma mortality where the “trend” seen is actually trends in treatment and access to care rather than trends in environmental influences.

- **Graphic displays.** All peer reviewers agreed that EPA should reconsider its graphical displays of reported new cases of disease. One reviewer stated strong opposition to the use of the log scale, noting that some trends become masked; discerning percent change in the reported number of cases is difficult using the current displays. The problem stems from trying to place very uncommon diseases such as cholera on the same scale as much more common afflictions. Reviewers recommended that, at a minimum, EPA present separate graphics for diseases with largely different reported numbers of cases.

References

[CDC] Centers for Disease Control and Prevention. 2005. Travel-Associated Dengue Infections—United States, 2001-2004. MMWR. 54(22):556-58.

2.5.2.6 Low Birthweight (LBW)

Reviewed by the Human Health Group

Consensus Statements	
Overall recommendation	**Include with modifications.**
Critical modifications	• Birth weight is a function of growth and gestational age. As constructed, LBW and preterm delivery indicators are not independent. Therefore, EPA should utilize a method that would track births that are small for gestational age (SGA). Recommended methods include tracking LBW (<2,500 grams) for term babies only or tracking births by LBW for gestational age (<10th percentile). • An important consideration is the growth of assisted reproductive technology; this technology is responsible for increased rates of multiple births. Because multiple birth babies tend to be SGA and are more frequently born preterm, EPA should monitor singleton births only. • EPA should include the 18-39 year age group only because women less than 18 years and those over 39 years have much higher rates of preterm birth and SGA babies, and because the rates of birth to such women are changing over time.
Suggested modifications	None.
Other comments	None.

The peer reviewers had a fairly lengthy discussion on the LBW indicator. In the end, all agreed that it was an appropriate and useful indicator. LBW is a component of the spectrum of adverse birth outcomes and an important risk factor for neonatal and postneonatal mortality. Further, two reviewers commented that some characteristics associated with LBW have strong environmental components, though htey acknowledged that many factors are unrelated to the environment. The reviewers questioned, however, whether the data were presented in the most meaningful way. Peer reviewers agreed unanimously that the indicator be retained, but only if EPA presents the data to clearly focus on growth, which would separate the LBW indicator from the pre-term delivery indicator. A summary of the discussions leading to peer reviewer conclusions and recommendations is presented below.

- One reviewer expressed strong views that, as presented, the indicators for LBW and preterm delivery are nearly identical given the strong association between birthweight and weeks gestation. Therefore, EPA should identify a method that would track births that are small for gestational age. Tracking low birthweight only among term births would be the simplest approach. Or, EPA could categorize births as being at or below the 10^{th} percentile for weight for gestational age (or small for gestational age). The other reviewers generally agreed. One reviewer cautioned, however, about the use of a non-parametric indicator such as <10% for gestational age: one will likely end up with an indicator that, in the aggregate, represents nothing more than the birthrate. EPA could achieve a parametric measure by categorizing gestational ages, then choosing a cutoff value (e.g., <1,500 grams for gestational age between 25 and 30 weeks). Trends in such data could then be used as indicators of effects on different subgroups.

- The same reviewer emphasized that LBW is also greatly influenced by many other factors, most notably the age of the mother and whether the birth is single or multiple. Because the increasing rates of and highest risk of LBW occurring in the very young or in women toward the end of their reproductive potential, this reviewer recommended that EPA's focus for the LBW indicator be on mothers between the age of 18 and 39 years. One reviewer argued that women over the age of 40 years have had greater environmental exposures and therefore statistics for this age group would be of interest to EPA. This reviewer recommended reporting statistics on the <18 and >39 year age groups, but doing so separately. These age groups may display more sensitivity and thus may act as early sentinels for environmental effects.

  In addition, the growing use of assisted reproductive technology has also had a sizable impact on birthweight for gestational age (Martin et al., 2005); the associated multiple birth babies tend to be smaller and come earlier. Therefore, from an environmental perspective presenting data for singleton births only makes more sense; it is cleaner and removes variability. Others agreed.

- Two reviewers questioned whether the LBW indicator should support the first (overall health status) or second (trends in diseases, conditions) question being posed in the health chapter. Another reviewer pointed out that four indicators related to birth outcomes are proposed for inclusion in ROE06: infant mortality, LBW, preterm delivery, and birth defects. Which are the best indicators? The group agreed that the LBW and infant mortality data are the strongest indicators; the birth defects database is the weakest. No conclusion was drawn in terms of whether the indicators were properly placed within the chapter.

References

Martin, JA et al. 2005. Annual summary of vital statistics—2003. Pediatrics; 115(3):619-34.

2.5.2.7 Birth Defect Incidence and Mortality

Reviewed by the Human Health Group

Consensus Statements	
Overall recommendation	**Include with modifications.**
Critical modifications	• Trends in birth defect mortality are influenced largely by access to and quality of medical treatment, not by incidence or environmental exposures. Therefore, EPA should place an emphasis on prevalence over mortality.
Suggested modifications	• EPA should refer to the data as prevalence data, not incidence data. • Birth certificates tend to be incomplete (e.g., approximately 40% of actual birth defects are missed); therefore, the overall quality of the underlying indicator data was questioned. There are two problems: 1) across the country, birth defects data are recorded incompletely and inconsistently on birth certificates, and 2) a significant portion of major birth defects are identified after a newborn is discharged from the hospital so that they will not be on the birth certificate. State birth defects registries identify these birth defects by reviewing hospital discharges during the first 12 months of life and provide a more complete assessment of birth defects prevalence. EPA should include birth defect prevalence as an indicator, but seek better-quality data sets: o EPA should work with the National Birth Defects Monitoring Network on developing a better indicator of birth defects prevalence. EPA should determine whether state efforts under this network can be used in this report, analogous to SEER. o EPA should identify subcategories of birth defects to track (neural tube defects, genitourinary, cardiac, cleft lip and palate, etc.).
Other comments	• EPA should track individual developmental disabilities (most notably ADHD, dyslexia and other learning disabilities, cerebral palsy, mental retardation, autism), as well as malformations. EPA should draw on the best available data whether from government or nongovernmental sources (e.g., March of Dimes). If the data are not currently available, EPA should encourage data collection to meet this information need. CDC's National Center on Birth Defects and Developmental Disabilities should be a partner in this. Developmental disabilities should be a separate indicator from birth defects. These recommendations are important because advances in the science of developmental toxicology are enhancing our understanding of the influence of environmental toxicants on developmental effects (NRC, 2000).

The peer reviewers agreed unanimously that Birth Defect *Prevalence* (not Birth Defect *Incidence*) is a useful indicator (see Shulman et al., 1988). Many conditions can be attributed to environmental or occupational exposures, though reviewers acknowledged that some linkages are stronger than others and other risk factors exist. Reviewers recommended, however, that Birth Defect Prevalence be emphasized over Birth Defect Mortality. Further, all agreed that EPA should seek better quality data sets and track specific types of birth defects. The basis for reviewer recommendations is presented below.

- **Indicator label.** The reviewers agreed that EPA should refer to birth defect "prevalence"—the statistic generally used for this outcome—not prevalence rate, incidence, or incidence rate.
- **Tracking birth defect prevalence over mortality**. Peer reviewers agreed that overall trends in birth defect mortality are shaped largely by improvements in treatment rather than changes in risk factors. Though all agreed that Birth Defect Prevalence is therefore a more meaningful indicator than Birth Defect Mortality, reviewers expressed varied views on whether to both should be retained as indicators. One reviewer expressed a strong opinion that mortality is not a good indicator of birth defects: most birth defects are not expected to lead to death (e.g., cleft palate). Another reviewer acknowledged that those who have tracked birth defect mortality show flatter curves than for birth defect prevalence, but this reviewer was not convinced that mortality should be eliminated completely; this outcome is different from asthma, for example—it still tells us something.
- **Using birth certificate data to track birth defects**. One reviewer emphasized that birth certificates are incomplete and may not be the best source for birth defect data (see Hexter et al. 1990). Even birth defects diagnosed immediately at birth can be greatly undercounted and underreported. More importantly, many significant birth defects are not diagnosed at birth and therefore not reflected on the birth certificate (e.g., developmental delays, neuromuscular defects). Also, the process for recording birth certificate information has weaknesses; quality assurance and followup are often lacking. Birth certificate recording is further complicated by the existence of multiple International Classification for Diseases (ICD) codes that include minor birth defects and deformations as well as major malformations. The same reviewer mentioned that a national system of birth defects registries is being developed that will ultimately provide a potentially better source of birth defects data. Registries follow children for the first year of life and track physical malformations and deformations. EPA should work with groups such as the National Birth Defects Monitoring Network to identify and build a better set of prevalence data. Other reviewers shared the above-stated concerns, but acknowledged that birth certificate records appear to represent the best available data and did not recommend eliminating this indicator in the absence of a better data set.
- **Tracking specific birth defects**. As data become available, peer reviewers agreed that EPA should track specific birth defects (neural tube defects, genitourinary, cardiac, cleft lip and palate, etc.).
- **Other comments**. One peer reviewer raised the concern about environmentally related developmental disabilities and suggested that they be tracked in addition to malformations/deformations—disabilities such as attention deficit hyperactivity disorder (ADHD), dyslexia and other learning disabilities, cerebral palsy, mental retardation, and autism. A short discussion followed and the other reviewers agreed that this is an important topic and, therefore, a possible new indicator for EPA consideration. The reviewers recommended that EPA collaborate with governmental and nongovernmental bodies to identify the best available data. Lastly, if the data are not available, the group encouraged EPA to partner with the CDC's National Center on Birth Defects and Developmental Disabilities to promote data collection for future tracking.

References

[NRC] National Research Council. 2000. Scientific Frontiers in Developmental Toxicology and Risk Assessment. National Academy Press, Washington, DC.

Hexter AC, Harris JA, Roeper P, Croen LA, Krueger P, Gant D. 1990. Evaluation of the hospital discharge diagnoses index and the birth certificate as sources of information on birth defects. Public Health Rep;105(3):296-307.

Schulman J, Shaw G, Selvin S. 1988. "Rates" of birth defects [see comments]. Teratology;38(5):427-9.

2.5.2.8 Childhood Cancer Incidence and Mortality

Reviewed by the Human Health Group

Consensus Statements	
Overall recommendation	**Include with modifications.**
Critical modifications	None.
Suggested modifications	• EPA should be tracking cancer incidence and not mortality. Trends in mortality are largely influenced by advances in treatment, not by incidence or environmental exposures. • EPA should track organ-specific cancers instead of overall cancer incidence. EPA should consider the following cancers: leukemia, brain, neuroblastoma, Wilms tumor, non-Hodgkins lymphoma (NHL), and bone, as well as other significant childhood cancers. Specify the primary site of origin only (e.g., leukemias), not the sub-type (e.g., acute myelocytic leukemia).
Other comments	None.

Peer reviewers discussions on this indicator were brief. The group was unanimous in its opinion that the Childhood Cancer Incidence (not Childhood Cancer Mortality) is an appropriate and useful indicator for evaluating human health. Environmental exposures are known or suspected to increase the risk of childhood cancer. The reviewers strongly recommended, however, that EPA's focus shift to cancer incidence and that organ-specific cancers be tracked instead of overall cancer incidence. Specific peer reviewer comments and recommendations follow.

- As discussed for some of the other health outcome indicators, peer reviewers agreed that incidence is a better measure of childhood cancer than mortality. As noted previously, reviewers emphasized that improvements in treatments, not changes in exposures or other triggers, shape the trend in mortality. *[See also peer reviewer responses to General Question 1 for additional opinion on the limitations of using mortality data.]*
- Two reviewers noted and the others agreed completely that childhood cancer should be tracked separately from adult cancers. Childhood cancers are dissimilar to cancers in adults. More of the cancers are from embryonic origin and affect different anatomic sites.
- One reviewer suggested that, at a minimum, EPA present data for the two most common primary cancer sites for children: leukemia and brain. Others suggested that EPA consider other notable childhood cancers, such as neuroblastoma, NHL, Wilms tumor, and bone cancer. The group agreed that EPA should include the primary cancer site only. In addition, the indicator write-up should discuss the multiple causal factors and the proportions of childhood cancers that most commonly occur.
- One reviewer recommended that the indicator write-up stress more recent understanding of carcinogenesis in children, including mention of how gene/environment interactions appear to be involved.

2.5.2.9 Childhood Asthma Mortality and Prevalence

Reviewed by the Human Health Group

Consensus Statements	
Overall recommendation	**Do not include.**
Critical modifications	• EPA should combine adult and childhood asthma into a single indicator. The disease is a continuum over a lifetime. Most adult asthma can be traced to early life exposures, with the exception of occupational triggers.
Suggested modifications	• EPA should display demographic breakdown, including race and ethnicity data. • EPA should present the childhood asthma prevalence in smaller age categories (now 0-17 years) because the prevalence is higher in younger children and because rates in younger children (0-4 years) may be a more sensitive indicator of environmental change. • In terms of the indicator itself: o EPA should be tracking asthma prevalence and not mortality. Trends in asthma mortality are influenced largely by advances in treatment, not by prevalence or environmental exposures. Although environmental conditions exacerbate asthma, most asthma-related deaths are completely preventable with appropriate medical treatment. With asthma, prevalence and attack are more related to the environment (both ambient and indoor). o Because the asthma case fatality rate is low, trend data for asthma mortality are not robust, especially when broken down into 10 EPA regions. This underscores the reviewers' recommendation not to track mortality.
Other comments	None.

Peer reviewers agreed unanimously that EPA should not include Childhood Asthma Mortality and Prevalence as a separate indicator. Instead, the group agreed that adult and childhood asthma be combined as a single indicator. See the summary of peer reviewer discussions on this topic under Asthma Mortality and Prevalence above.

2.5.2.10 Preterm Delivery

Reviewed by the Human Health Group

Consensus Statements	
Overall recommendation	**Include with modifications.**
Critical modifications	• An important consideration is the growth of assisted reproductive technology; this technology is responsible for increased rates of multiple births (citation to be added). Because multiple birth babies tend to be SGA and are more frequently born preterm, EPA should monitor singleton births only. • EPA should include the 18-39 year age group only because women younger than 18 or over 39 have much higher rates of preterm birth and SGA babies, and because the rates of birth to such women are changing over time.
Suggested modifications	• In the indicator discussion, EPA should acknowledge that the causes of preterm births are not fully known; they are multi-factorial and are believed to include environmental factors.
Other comments	None.

Peer reviewer discussions of the Preterm Delivery indicator occurred concurrently with those related to the LBW indicator. The reviewers all agreed that overall the indicator should be included, but not before questioning its relative importance as a health indicator in EPA's report on the environment. An overview of peer reviewer discussions on this topic follows:

- Three reviewers initially questioned the strength of Preterm Delivery as an indicator of environmental effects. Multiple factors are related to preterm delivery, such as genetics, dietary choices, hypertension, stress, or strenuous physical labor. The importance of environmental associations is less clear, but cannot be ruled out. All of the peer reviewers agreed that the EPA's indicator write-up needed to more clearly state these points.
- For the same reasons as described for the LBW indicator, one reviewer strongly recommended that EPA only present preterm delivery statistics for mothers between the age of 18 and 39 years. Again, one reviewer argued that women over the age of 40 years have had greater environmental exposures and therefore statistics for this age group would be of interest to EPA.
- As with LBW, one reviewer strongly recommended looking at singleton births only for a cleaner presentation of data and to reduce variability. Others agreed.
- Where possible, one reviewer recommended presenting race/ethnic trends separately. Another reviewer commented that the overall trends presented are informative, but suggested an alternative presentation of the regional data.

2.5.3 BIOMEASURES OF EXPOSURE

2.5.3.1 Blood Lead Level

Reviewed by the Human Health Group

Consensus Statements	
Overall recommendation	**Include with modifications.**
Critical modifications	None.
Suggested modifications	• The inclusion of demographic data in Table 098_105Lead serves as a good model for other indicators, but a graphical display of race and ethnicity trends would be easier to read. • EPA should display available temporal trend data (e.g., plot the 1-5 year group over time); much data exist.
Other comments	None.

The peer reviewers agreed unanimously that Blood Lead Level is an appropriate and useful indicator for evaluating trends in exposures to lead. Biomonitoring data are useful in understanding the extent to which people are exposed and can be used to illuminate underlying environmental trends. Further, lead exposure comes from environmental contamination. Because lead has been so widely studied, the reviewers recommended that EPA include more extensive temporal trend data. The reviewers recommended obtaining data from earlier NHANES reports and other appropriate sources. One reviewer expressed greater interest in showing more recent trends and trends in NHANES "regions" (e.g., northeast southwest, inner city, rural).

2.5.3.2 Blood Mercury Level

Reviewed by the Human Health Group

Consensus Statements	
Overall recommendation	**Include with modifications.**
Critical modifications	None.
Suggested modifications	• Male exposure data are not presented, which represents a hole in the data set. Mercury is associated with other outcomes (e.g., cardiovascular disease, hypertension, immune system effects). EPA should present data for males as well as females, although reviewers agree with providing a breakout of women of childbearing age. • The inclusion of demographic data in Table 098_105Lead serves as a good model for other indicators, but a graphical display of race and ethnicity trends would be easier to read. • Where available, EPA should display temporal trend data.
Other comments	None.

The peer reviewers agreed unanimously that Blood Mercury Level is an appropriate and useful indicator for evaluating trends in exposure to mercury and in evaluating human health. Peer reviewers discussed this indicator only briefly, but identified the lack of male exposure data as a notable gap in the indicator because adverse health effects associated with mercury exposures have been documented in males and females. One reviewer cited two examples from the scientific literature: Beuter and Edwards (2004) and Yokoo et al. (2003). Health effects possibly associated with mercury exposure across the population include cardiovascular disease, hypertension, and immune system effects, among others. Another reviewer mentioned studies looking at lower intelligence scores in mercury-exposed individuals and resulting loss in productivity (Trasande et al. 2005).

As noted for other indicators, the peer reviewers agreed that EPA should display temporal trend data where possible.

References

Beuter A and Edwards R. 2004. Effect of chronic exposure to methylmercury on eye movements in Cree subjects. Int Arch Occup Environ Health; 77(2):97-107.

Trasande L, Landrigan PJ, Schechter C. Public health and economic consequences of methyl mercury toxicity to the developing brain. Environ Health Perspect. 113(5):590-6.

Yokoo EM et al. Low level methylmercury exposure affects neuropsychological function in adults. Environ Health; 2(1):8.

2.5.3.3 Blood Cadmium Level

Reviewed by the Human Health Group

Consensus Statements	
Overall recommendation	**Include.**
Critical modifications	None.
Suggested modifications	• EPA should acknowledge that cadmium data from CDC's Second National Report on Human Exposure to Environmental Chemicals represent one point and time; only as more data become available can longer-term trends be tracked.
Other comments	None.

The peer reviewers agreed unanimously, with little discussion, that the basis for including Blood Cadmium Level as an indicator is valid because cadmium has multiple environmental sources, no endogenous source, a long half-life, known renal toxicity, and a known mechanism of action, and is a potential endocrine disruptor. One reviewer pointed out that we do not know, however, the extent to which blood cadmium concentrations are mitigated by genetic predisposition—a factor that would affect measured levels under similar exposures.

The peer reviewers agreed that the National Health and Nutrition Examination Survey (NHANES) data provide a reasonable unbiased estimate of the presence of this biomarker across the population. The group acknowledged, however, that data from CDC's Second National Report on Human Exposure to

Environmental Chemicals presented for peer review represent only one point and time. Therefore, the reviewers recommended that EPA clearly explain that only in the future can trends be tracked.

2.5.3.4 Blood Persistent Organic Pollutants (POPs) Level

Reviewed by the Human Health Group

Consensus Statements	
Overall recommendation	**Include.**
Critical modifications	None.
Suggested modifications	• EPA should acknowledge that POP data from CDC's Second National Report on Human Exposure to Environmental Chemicals represent one point in time; only as more data become available can longer-term trends be tracked.
Other comments	None.

The peer reviewers agreed unanimously, with little discussion, that the basis for including Blood POPs Level as an indicator is valid because POP exposure comes from environmental sources, can reflect recent or current exposures, and some POPs have been associated with increased risk in disease and endocrine disruption. One reviewer pointed out that we do not know, however, the extent to which blood POP concentrations might be mitigated by genetic predisposition thus affecting measured levels under similar exposures. Another reviewer pointed out that the release of some POPs to the environment has decreased in this country; however, POPs are not being controlled and global occurrence has not ceased. Therefore, the peer reviewers agreed that monitoring possible exposure trends is important.

The peer reviewers agreed that the National Health and Nutrition Examination Survey (NHANES) data provide a reasonably unbiased estimate of the presence of this biomarker across the population. The group acknowledged, however, that data from CDC's Second National Report on Human Exposure to Environmental Chemicals presented for peer review represent only one point and time. Therefore, the reviewers recommended that EPA clearly explain that only in the future can trends be tracked.

2.5.3.5 Urinary Pesticide/Herbicide Level

Reviewed by the Human Health Group

Consensus Statements	
Overall recommendation	**Include with modifications.**
Critical modifications	None.
Suggested modifications	• EPA should rename the indicator "Urinary Pesticide Level," using the term pesticide only. Herbicides and insecticides are types of pesticides. • EPA should acknowledge that urinary pesticide levels are not a good clinical indicator of exposure due to generally short half-lives, but over a population urinary pesticide levels are a reasonable measure of exposure. However, measuring pesticide metabolites does not necessarily point to a specific pesticide exposure. • EPA should use, explain, and justify the use of creatinine-corrected data. • Both uncorrected and creatinine-corrected data do not need to be presented. Reviewers believe that the creatinine-corrected data are modestly better and, therefore, EPA should present the corrected data only. • EPA should provide age, race, and ethnicity breakdowns. • EPA should include new pesticide data available in CDC's Third National Report on Human Exposure to Environmental Chemicals, including pyrethroids.
Other comments	None.

The peer reviewers agreed unanimously that Urinary Pesticide/Herbicide Level is an appropriate and useful indicator. Pesticide metabolites in the urine represent a measure of environmental exposure, making it an important marker. Peer reviewers acknowledged, however, the somewhat non-specific nature of this measure and the fact that it represents recent exposures only. The group had relatively brief discussions about the overall usefulness of this indicator, identifying some key limitations and making recommendations for modifying the indicator analysis and write-up. A summary of peer reviewer discussions and the basis for their recommendations is presented below.

- **Indicator name.** One peer reviewer voiced surprise that the indicator is not simply labeled "Urinary Pesticide Level," since herbicide is a category of pesticide. All agreed that it should be renamed as such.

- **Utility of the indicator.** Two peer reviewers expressed some reluctance to rely on urinary pesticide metabolite levels—generally indicative of recent exposures only—to measure trends in exposure or assess disease potential. One of these reviewers specifically cautioned about taking values reported below the "limit of detection" at face value because these compounds do not persist in the body. Also, measuring metabolites does not enable a "true" measure of pesticide exposure: metabolite concentrations can be mitigated by genetic predisposition, affecting measured levels under similar exposure scenarios. Another reviewer agreed that the measure does not always serve as a good clinical indicator, but said it is a reasonably good indicator for understanding overall population trends. All agreed that the short-lived nature of these metabolites is a shortcoming and needs to be

clearly acknowledged in the indicator write-up. In addition, the peer reviewers acknowledged that the metabolites are not specific to a particular pesticide; this too needs to be clearly noted in the indicator discussion, they said.

- **Presenting creatinine-corrected data.** Peer reviewers debated the pros and cons of presenting uncorrected versus creatinine-corrected data (which account for the effects of dilution and other factors). After a brief discussion of what each represents, the group agreed that both do not need to be presented and recommended that EPA consider including corrected data only. One reviewer noted, however, that corrected data are better for adults, but not necessarily growing children. Overall, reviewers agreed that the creatinine-corrected data are modestly preferable to the uncorrected data and that presentation of both sets of data did not add information (and therefore introduces an unnecessary layer of complexity). Most importantly, the group agreed that EPA's write-up should clearly explain what the creatinine-corrected data mean and why one set or both are used.

- **Age, gender, race/ethinicity breakdowns.** As for other indicators, the peer reviewers all agreed that EPA should consider presenting demographic breakdowns of the data when available. One reviewer was particularly interested in seeing metabolite data for children presented separately from those for adults; different characteristics in children could produce different metabolites than in adults. The reviewers noted, however, that such breakdowns are less important and less meaningful (and therefore undesirable) in cases where large numbers of "non-detects" are reported.

- **Including most recent NHANES data.** One reviewer pointed out, and others strongly agreed, that EPA should include recently released data from NHANES in ROE06. The reviewer specifically mentioned the pyrethroid data.

2.5.3.6 Phthalate Exposure

Reviewed by the Human Health Group

Consensus Statements	
Overall recommendation	**Include with modifications.**
Critical modifications	None.
Suggested modifications	• Rename the indicator "Urinary Phthalate Levels" for clarity and consistency with other biomeasure indicators. • EPA should use, explain, and justify the use of creatinine-corrected data. • Both uncorrected and creatinine-corrected data do not need to be presented. Reviewers believe that the creatinine-corrected data are modestly better and that, therefore, EPA should present the corrected data only. • EPA should include age, gender, and race/ethnicity data; particularly important are women of childbearing age because animal toxicity data indicate that *in utero* period could be a vulnerable window of exposure.
Other comments	• The reviewers acknowledged the comment from the American Chemistry Council, but disagree that the phthalate indicator should be eliminated. Exposure to phthalates is a rapidly emerging public health and medical concern and therefore must be given high priority by EPA. The reviewers recommend that the introduction to this indicator reference the National Toxicology Program (NTP) Center for the Evaluation of Risks to Human Reproduction review of these six phthalate compounds.

The peer reviewers agreed unanimously that Phthalate Exposure is an appropriate indicator for EPA consideration. Phthalates represent an important class of compounds that is ubiquitous in the environment. Further, these compounds may have potential reproductive effects, making them a high-priority group of compounds to track. The reviewers did recommend, however, that the indicator be renamed "Urinary Phthalate Level" for consistency with the other biomeasure of exposure indicators. The reviewers also provided some recommendations for modifying this indicator, as detailed below.

- **Presenting creatinine-corrected data.** Peer reviewers debated the pros and cons of presenting uncorrected versus creatinine-corrected data (which account for the effects of dilution and other factors). After a brief discussion of what each represents, the group agreed that both do not need to be presented and recommended that EPA consider including corrected data only. One reviewer noted, however, that corrected data are better for adults, but not necessarily growing children. Overall, reviewers agreed that the creatinine-corrected data are modestly preferable to the uncorrected data and that presentation of both sets of data did not add information (and therefore introduces an unnecessary layer of complexity). Most importantly, the group agreed that EPA's write-up should clearly explain what the creatinine-corrected data mean and why one set or both are used.

- **Age, gender, race/ethnicity breakdowns.** As for other indicators, the peer reviewers all agreed that EPA should consider presenting demographic breakdowns of the data when available. Of particular interest is separating out women of childbearing age: exposures *in utero* are believed to represent a vulnerable window of exposure based on animal studies. The reviewers noted, however, that such

breakdowns are less important and less meaningful (and therefore undesirable) in cases where large numbers of "non-detects" are reported.

- **Data displays.** One peer reviewer commented that the data presentation was not sufficient. Because of the large number of markers with reported levels below the level of detection (e.g., mono-cyclohexyl phthalate and mono-n-octyl phthalate), it may provide greater perspective to include a pie chart displaying the relative contribution of the different phthalates.

- **Other comments.** The peer reviewers acknowledged the public comment from the American Chemistry Council suggesting that the phthalate indicator be eliminated, but all of the reviewers disagreed strongly with the council's recommendation and the rationale behind that recommendation. To emphasize the importance of this indicator, the reviewers recommended that EPA cite the NTP review on phthalates (Kavlock et al., 2002a-g) in the indicator write-up.

References

Kavlock, R et al. 2002a. NTP Center for the evaluation of risks to human reproduction: phthalates expert panel report on the reproductive and developmental toxicity of di-n-octyl phthalate. Reprod Toxicol. 16(5):721-34.

Kavlock, R et al. 2002b. NTP Center for the evaluation of risks to human reproduction: phthalates expert panel report on the reproductive and developmental toxicity of di-n-hexyl phthalate. Reprod Toxicol. 16(5):709-19.

Kavlock, R et al. 2002c. NTP Center for the evaluation of risks to human reproduction: phthalates expert panel report on the reproductive and developmental toxicity of di-isononyl phthalate. Reprod Toxicol. 16(5):679-708.

Kavlock, R et al. 2002d. NTP Center for the evaluation of risks to human reproduction: phthalates expert panel report on the reproductive and developmental toxicity of di-isodecyl phthalate. Reprod Toxicol. 16(5):655-78.

Kavlock, R et al. 2002e. NTP Center for the evaluation of risks to human reproduction: phthalates expert panel report on the reproductive and developmental toxicity of di(2-ethylhexyl) phthalate. Reprod Toxicol. 16(5):529-653.

Kavlock, R et al. 2002f. NTP Center for the evaluation of risks to human reproduction: phthalates expert panel report on the reproductive and developmental toxicity of di-n-butyl phthalate. Reprod Toxicol. 16(5):489-527.

Kavlock, R et al. 2002g. NTP Center for the evaluation of risks to human reproduction: phthalates expert panel report on the reproductive and developmental toxicity of butyl benzyl phthalate. Reprod Toxicol. 16(5):453-87.

2.5.4 RESPONSE TO GENERAL QUESTIONS

2.5.4.1 General Question 1: Relative Value and Importance of Indicators

Peer reviewers were asked whether, when considered collectively, any of the proposed indicators seem to be more appropriate, adequate, or useful for evaluating human health or in answering the health chapter questions. An overview of topics discussed over the course of the 3-day peer review meeting is presented below. This includes peer reviewer comments and recommendations related to (1) the overall usefulness of data sources, (2) the use of mortality data in general, and (3) evaluating regional trends using available national-scale indicator data. The overview also includes the results of a "ranking" exercise conducted on the last day of the peer review meeting.

- **Quality and adequacy of available data sources**. The peer reviewers reviewed the primary data sources used for the proposed health outcome and biomeasure indicators:
  - National Health and Nutrition Examination Survey (NHANES)
  - National Vital Statistics System (NVSS)
  - National Health Interview Survey (NHIS)
  - The Surveillance, Epidemiology, and End Results (SEER) Program
  - National Notifiable Diseases Surveillance System
  - American Association of Poison Control Centers (AAPCC)

  The peer reviewers agreed overall that the health indicators were drawn from the best available databases. The reviewers acknowledged that known biases and inherent weaknesses exist within and across some of these data sources and that some are stronger than others, but the reviewers did not determine that any were unsuitable for EPA use in ROE06. Important limitations of individual data sets identified by the peer reviewers during the meeting are described in the indicator-specific discussions presented above.
- **Use of mortality data**. Throughout their discussions on health outcome indicators, peer reviewers emphasized that in many or most cases incidence or prevalence data were preferred over mortality data. The reasons provided by peer reviewers follow.
  - Many factors other than environmental causes contribute to death (e.g., quality and access to medical care).
  - Limitations, weaknesses, and uncertainties are associated with the use of death certificate data. Indicator write-ups imply greater certainty than exists.
  - Mortality is a good reflection of incidence only under certain conditions. Mortality is only a good surrogate for disease incidence when the disease is highly lethal (e.g., pancreatic cancer).
  - For cancer, asthma, and birth defects, incidence or prevalence data should be used when available instead of mortality data. Trends in mortality for these diseases or conditions are more affected by advances in medical treatment than changes in the environment (e.g., childhood leukemia).

  In cases where EPA chooses to retain mortality data, the peer reviewers recommended that EPA emphasize incidence or prevalence over mortality and clearly describe the limitations, weaknesses, and uncertainties of mortality data sets.
- **Presentation of regional data**. The peer reviewers agreed that in most cases the regional breakout of data offered little additional insight to the indicator discussions. Peer reviewers communicated the following array of comments and recommendations on this topic.

- The group understands why EPA may want to track disease rates or conditions in its 10 regions, but several reasons exist that limit the utility of this exercise. Boundaries are established for policy reasons. Jurisdictional issues may be important, but pollution could be coming from anywhere. No possible links can be established with health status and environmental cause. An optimal breakdown would be to link health data with environmental exposure situations. EPA may want to consider aggregating the data in a more environmentally sensitive way (e.g., by urban area, watershed), but acknowledge that only NVSS has data down to county level. It might be possible to use NCHS SMSA categories (inner city, non–inner city, or rural), all based on Census bureau data.
- CDC's Environmental Health Tracking Program is aimed at addressing this issue, but currently only small-scale studies with varied approaches are in process.
- The group as a whole agreed that EPA should explore better ways to display regional data trends, if they are included at all. The graphics associated with the regional breakouts are difficult to read and do not add a lot of information. Exceptions exist, such as when one region plots consistently higher than the other regions (e.g., CVD mortality). One recommendation was to redesign plots and present more vertical versus horizontal plots.
- The group agreed that the concept of using maps is good, but data sets are broken out in quartiles and each quartile is not represented on the various maps. State-by-state breakouts would be better.
- Regional plots for cancer mortality are not especially useful.

- **Priority indicators**. As described in the indicator-specific discussions, peer reviewers agreed that EPA's proposed indicators generally met basic indicator criteria and helped to answer the questions that EPA is trying to answer. Peer reviewers offered some mixed opinions on which indicators were most important, but all stressed the fact the majority are appropriate and useful and should be retained. As was teased out during indicator-specific discussions and determined during a quick ranking of the indicators at the end of the meeting, the less important health indicators include life expectancy, general mortality (or crude death rate), low birthweight/preterm delivery, birth defect incidence and mortality, and blood POPs level. One reviewer commented that an imbalance of indicator groups existed, and that duplication should be reduced where possible (e.g., infant-related indicators). However, most reviewers indicated that the mix and number of indicators were appropriate. In trying to rank the indicators, the group emphasized for the record that they were not attempting to reduce the number of indicators. Rather, as directed, the group attempted to provide a relative sense of indicator importance.

2.5.4.2 General Question 2: Proposed New Indicators

Peer reviewers were asked whether they recommended any additional national-level indicators that make an important contribution to answering the health chapter questions, but were not proposed for ROE06. The group reviewed EPA's list of withdrawn indicators and recommended that EPA consider retaining the following indicators, most of which are non–health chapter indicators. Peer reviewer pre-meeting comments provide greater detail on individual rationale.

- *CVD prevalence*. As noted in the CVD indicator section above, the peer reviewers agreed that EPA should include CVD prevalence. Prevalence is a better indicator of CVD than mortality.
- *Production of ozone-depleting substances*. The group agreed this was an important indicator and did not understand why it was withdrawn.
- *Number of people living in counties with ambient air conditions above NAAQS*. Most of the peer reviewers disagreed with EPA's rationale for the withdrawal of this indicator. Specifically, the

reviewers argued that the indicator should not be withdrawn on the basis that it is not an "actual marker of exposure measured on individuals" or because people are moving. The bar is being set too high. Personal monitors are not needed to measure exposure and in fact would be too burdensome and expensive. Crude ambient measures are adequate for tracking exposure. Further, the rationale given for removing this indicator could be applied to many other indicators that are not an "actual marker of exposure to individuals," yet they are retained.

- *Percentage of homes with smokers*. As noted during the Blood Cotinine Level discussions, peer reviewers all agreed that tracking the number of homes with smokers was a good indicator. This indicator provides more information than blood cotinine alone—that is, information on the exposure source. Further, reviewers disagreed with EPA's rationale that data collection methods were questionable, especially given that other data accepted by EPA (e.g., asthma prevalence) are derived in precisely the same way (via a national population based survey).
- *Pesticide usage.* The peer reviewers agreed that understanding trends in pesticide usage is important to learning what populations and indicators are most relevant (e.g., biomeasures for pesticides with short half-lives would be less meaningful if usage has declined). Therefore, the reviewers recommended retaining this indicator, but recommended disaggregating the data. In particular, the disaggregation should result in making the specific classes of pesticides more transparent. One reviewer noted, for example, that it will be interesting to follow the phase-out of organophoshate pesticdes and the phase-in of pyrethroids.

Peer reviewers agreed that the following indicators not be included in ROE06, but recommended ways to improve and use such data in the future.

- *Beach days/beach advisories/contaminants of streams and groundwater*. The peer reviewers disagreed with EPA's reason for omitting this indicator. They agreed, however, that these indicators should not be included because of data consistency in data collection efforts across states (data not comparable across time and space); they agreed that EPA should explore ways to improve consistency and establish better mechanisms both for monitoring the healthfulness of the nation's waters for swimming and for tracking this important information.
- *Radioactive waste storage and disposal*. The peer reviewers recommended that EPA reexamine possible ways to use the data in light of limited access to pertinent Department of Energy data.
- *Blood VOC and urinary arsenic*. The peer reviewers recommended that EPA continue to work with other agencies (e.g., CDC) to build data sets.
- *Animal deaths and deformities*. The reviewers agreed that this could be an important (sentinel) indicator for human health. What happens in animals could be a good indicator of what happens in humans. After discussing the source and reliability of this data set with reviewers of the ecological chapter, the health reviewers agreed that EPA should continue to work with the appropriate federal agencies (e.g., U.S. Fish & Wildlife) to learn more about national and regional programs collecting such data, with the goal of identifying better data and establishing more systematic tracking mechanisms. Regarding the data set supporting this withdrawn indicator, the health reviewers noted that the lack of precise counts and unknown causes were not as much of a concern to them as the possible inconsistent data collection methods over time, small numbers, and lack of validation information on whether such data reflect overall trends. For example, infectious disease tracking data are also based on "indicator" reporting of cases by the medical system to government but the CDC and the states have produced studies that indicate that these systems to produce valid measures of trends, even though they do not capture all the cases of such diseases.

In addition to discussing the withdrawn indicators, peer reviewers agreed that the following new indicator should be considered.

- *Developmental disabilities*. As discussed during birth defects deliberations, the peer reviewers recommended tracking developmental disabilities (e.g., ADHD, dyslexia, cerebral palsy, mental retardation, autism) as well as malformations. EPA should search for available data sets and if data are not currently available, EPA should encourage data collection to meet this information need. The CDC National Center on Birth Defects and Developmental Disabilities should be a partner in this. Developmental disabilities should be a separate indicator from birth defects. One reviewer noted that a child would need to be followed to at least age 12 for this indicator to be useful.

Other indicators discussed but for which no consensus was reached are listed below.

- *Housing starts.* One reviewer recommended that EPA consider adding indicators that address land use, many of which have negative environmental impacts. In conjunction, EPA may want to consider monitoring energy consumption associated with large homes.
- *Urban renewal.* One reviewer suggested that data tracking urban renewal activities would be a good complement to housing starts, though it is unclear whether a good metric exists. One reviewer noted that Howard Frumkin, NCEH/ATSDR, has done work in this area.
- *Poverty index*. The reviewers discussed topics related to the appropriateness of measuring socioeconomic status at relative length. Two reviewers commented that measuring poverty as a potential measure for higher environmental exposures is not appropriate, citing work by Gwynn and Thurston (2001) and others as supporting this premise. Health care and health access is the issue, not disproportionate exposure. An exception may be housing and lead. [*See also general comments below on whether EPA should track poverty level in addition to other demographic data when presenting health indicators.*]
- *Antibiotics in water*. One peer reviewer questioned tracking the levels of antibiotic releases as a potential problem. Others stated that no levels of health significance have been reported.

Reference

Gwynn RC and Thurston GD. 2001. The burden of air pollution impact on racial minorities. Environ Health Persp; 109:501-5.

2.5.4.3 Other General Comments

Throughout the course of discussions, peer reviewers offered various comments that apply across indicators or do not fit into any specific discussion topic presented in previous sections. These are summarized below.

- If they are available, EPA should consistently include age, gender, race, and ethnicity breakdowns when presenting indicator data (tables and graphical displays). In some cases, such breakdowns may be less important and could be excluded (e.g., biomeasure data for which reported levels are largely below the level of detection). In addition, EPA should include temporal trend data when they are available.
- The peer reviewers questioned whether EPA also should include data related to poverty level in addition to the gender, race, and ethnicity breakdowns mentioned above. No consensus was reached.

Two peer reviewers noted that they would support including poverty level data. The others questioned how much epidemiology the agency should do and suggested not including the poverty level data. It was further noted that this information is not available across data sets. For example, NHANES has compiled poverty level data, but NVSS and SEER have not.

- One reviewer commented that materials for peer reviewer examination emphasized data accuracy and collection over use and interpretation by EPA. There is no clear connection between indicators and efforts at EPA to prevent disease or improve health. The group acknowledged that the non-indicator text is expected to address this issue to some extent and is beyond the purview of this peer review.
- One reviewer recommended using the categories used by the International Panel on Climate Change (IPCC) in the context of the health indicators. Another reviewer disagreed, emphasizing that EPA is not proving cause and effect.
- All the peer reviewers agreed that the level of detail and encyclopedic nature of the information presented in draft ROE03 should serve as a model for ROE06. One reviewer commented, and others agreed, on the importance of identifying important indicators to carry through to the future.
- One reviewer questioned the extent to which EPA will be able to update ROE as new data become available. EPA responded that e-ROE is being established to enable such updates. The peer reviewers fully supported this approach.